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EXAMINER

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ART UNIT	PAPER NUMBER
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1652

13

DATE MAILED: 12/13/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/502,498

Applicant(s)

KILIAN ET AL.

Examiner

Malgorzata A. Walicka

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 October 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4,6,7,9-19,22-27,29,31-44 and 46-64 is/are pending in the application.
- 4a) Of the above claim(s) 1-4, 6-7, 9-15, 23-28, 29, 31-44, and 46-64 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 16-19 and 22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: copies of the relevant pages of the US Pat. No. 6,093,809.

The examiner acknowledges the Preliminary Amendment filed February 11, 2000. Claims 5, 8, 20, 21, 28, 30 and 45 have been cancelled. Claims 3, 4, 6, 7, 9, 11, 13, 18, 27, 28, 29, 31, 33, 34, 36, 37, 44 and 53 have been amended as requested. Filing of the Supplemental Preliminary Amendment, the Sequence Listing, on Oct. 13, 2000 is acknowledged. The amendment was entered.

In Amendment and Response to Restriction Requirement filed on October 30, 2001, paper No. 12, Applicants elected, with traverse, claims 16-19 and 22 of Group II, drawn to vertebrate telomerase, its variants and fragments. In response to the requirement of species election Applicants elected the variant described by SEQ ID NO:46.

Claims 1-4, 6-7, 9-19, 22-27, 29, 31-44 and 46-64 are pending in the application; claims 16-19 and 22 are the subject of this Office action; claims 1-4, 6-7, 9-15, 23-28, 29, 31-44 and 46-64 are withdrawn from consideration as drawn to the nonelected invention.

Detailed Office Action

1. Restriction/Election

In response to the restriction requirement, paper No. 8, mailed on May 30 2001, Applicants elected, with traverse, Group II claims 16-22, however claims 20 and 21 were cancelled by the preliminary amendment, therefore Group II comprises claims 15-19 and 22.

The Applicants traverse the restriction requirement as it applies to Group I-VI. The traverse is on the ground that the examiner has failed to make a showing that the

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search and examination of these groups would entail a serious burden. Applicants also argue that the reasons for the independence of the inventions of particular groups are stated merely conclusory.

Applicants are kindly reminded that restriction involves four factors: distinctness, independence, classification and burden to the examiner.

Protein and DNA encoding said protein (Group I and II) are distinct chemical entities and require different searching of patent and non-patent literature as revealed by their different classification. Though the searches are overlapping, they are not coextensive. Search of Group I would require search for host cell transformed with the expression vector, class 435, subclass 252.3 as well as class 536, subclass 23.2 encompassing DNA encoding enzymes. Search of these classes is unnecessary for the search of Group II that is classified in class 435 subclass 194. Thus, due to different classification, independence and different literature search restriction between Group I and Group II is proper. Group III is classified in class 530, subclass 387.9 is drawn to antibody to the vertebrate and hybridoma calls for their production. Group IV is classified in class 536, subclasses 24.3 and 24.1. Inventions of Group I-VI are not only classified in distinct classes, but also are distinct or independent for reasons stated clearly in the restriction requirement, paper No. 8. However, to advance the prosecution the examiner withdraws the restriction between Groups V and VI. Thus, the revised restriction requirement encompasses the following groups:

- I. Claim 1-4, 6, 7, 9-15 and 61, drawn to DNA, expression vector and transformed host cell to produce recombinantly vertebrate telomerase, classified in class 435, subclass 252.3.

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- II. Claim 16-19 and 22, drawn to vertebrate telomerase, its variants and fragments, classified in class 435, subclass 194.
- III. Claim 23-26, drawn to antibody and a hybridoma cell for their production, classified in class 530, subclass 387.9.
- IV. Claim 27, 29, 31-40, drawn to the telomerase DNA probe, primers for amplification, and oligonucleotides that hybridize to telomerase gene, classified in class 536, subclasses 24.3 and 24.1.
- V. Claim 41-44, 46-47 and 48-49, drawn to a method of diagnosing cancer using telomerase cDNA, and a pattern of expression of telomerase RNA, classified in class 435, subclass 6.
- VI. Claim 50-53, drawn to transgenic animals where the telomerase gene is operably linked to a promotor effective for the expression of the gene, classified in class 800, subclass 13.
- VII. Claim 54, drawn to a mouse having endogenous telomerase gene disrupted, classified in class 800, subclass 9.
- VIII. Claim 55-59, drawn to inhibitor of vertebrate telomerase, classified in class 435, subclass 184.
- IX. Claim 60, drawn to a method of treating cancer, comprising administering therapeutically effective amounts of telomerase inhibitor, classified in class 514, subclass unknown.
- X. Claims 62-64 drawn to a method of identifying an effector of telomerase activity classified in class 536, subclass 184.

In conclusion, the Applicants' arguments have been found persuasive only as to rejoining of Group V and VI. The new restriction as written above is proper for reasons presented in the previous restriction requirement, paper No. 8, and is made FINAL. Elected claims 16-19 and 22 of Group II are examined on merits.

2. Objections

2.1. Specification

The usage of terms exon and intron is confusing in specification. The specification refers, on page 19, line 19 and further, to telomerase variants presented in Figure 7: "exons are deleted (see α , β , Fig. 7)." Also in the figure fragments Y, α and β are described as "exon(s) delated." On the other hand, fragments Y, 1, α , β , 2, 1, and X are called introns in the Sequence Listing (SEQ ID NO:18, 23, 25, 27, 29, 32).

2.2. Drawings

Figure 7 is illegible and confusing as to the usage of the terms exon and intron; see above. Position of fragment X is not marked in the figure.

Figure 10A presents two sequences labeled as "**". The "**" sequence consisting of 36 bases is in the Sequence Listing (page 21) labeled as intron α , SEQ ID NO:25. Please use identifying and clear labels.

Figure 7 is illegible and, in addition, confusing as to the usage of the terms exon and intron; see above. Position of fragment X is not marked in this figure.

2. Rejections

2. 1. 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 19 and 22 are confusing because they recite the term "a portion of a vertebrate telomerase" or a "portion of claim 19." For examination purposes it is assumed the claim 19 and 22 refers to a fragment of a vertebrate telomerase protein.

2.3. 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2.3.1. Lack of written description

Claim 19 and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are directed to any fragment or any 10-100 amino acid fragment of any vertebrate telomerase protein. The genus of claimed polypeptides is a large variable genus, because there is an extremely large number of species of vertebrate and telomerase proteins that may be isolated from them. The number of any size fragments or the 10-100 amino acid fragments that may originate from those telomerases is even greater. The only species of such polypeptides taught by the specification are polypeptides that may be encoded by sequences that are introns of the human telomerase (SEQ ID NO:18, 23, 25, 27, 29, 32 and 33). However, the specification fails to describe any other representative species

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by any identifying characteristics or properties other than being fragments of a vertebrate telomerase. Also, neither special functional or structure features of said fragments are disclosed. In view of lack of any functional and structural characteristics of the fragments, as well as the vertebrate species encompass by the scope of the claims, Applicants failed to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize they were in possession of the claimed invention.

Claim 18 is rejected because the claim is directed to a large and variable genus of proteins that are variants of SEQ ID NO:46. Disclosure teaches only one species of the claimed genus, i.e. SEQ ID NO:46, without any identifying characteristics of the other species. The scope of the claim encompasses an extremely large number of proteins having sequences generated by substitution, deletion and/or insertion of any amino acid residue with any amino acid and/or any number of any amino acids. The applicants did not describe how to modify protein of SEQ ID NO:46 to obtain the claimed variants. Also, Applicants did not set forth any special functional and structural features of claimed variants. In the view of the lack of any structural and functional characteristics of the variants encompassed by the scope of the claim, Applicants failed to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize they were in possession of the claimed invention.

2. 3.2. Scope of enablement

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Claims 16, 19 and 22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the variant of human telomerase described by SEQ ID NO:46 and its fragments that may be encoded by the introns (SEQ ID NO:18, 23, 25, 27, 29, 30, 32 and 33), does not reasonably provide enablement for any vertebrate telomerase, its fragments or fragments that are 10-100 amino acid in length. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The claims are broader than the enablement provided by the disclosure with regard to the extremely large number of: 1) all known and unknown enzymes having said activity and originating from all vertebrates, 2) fragments of any vertebrate telomerase or fragments that are of 10-100 amino acid in length. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Otherwise, undue experimentation is necessary to make the claimed invention. Factors to be considered in determining whether undue experimentation is required, are summarized *In re Wands* [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the nature of the invention, (b) the breadth of the claim, (c) the state of the prior art, (d) the relative skill of those in the art, (e) the predictability of the art, (f) the presence or absence of working example, (g) the amount of direction or guidance presented, (h) the quantity of experimentation necessary.

The nature and breath of the claimed invention encompasses any telomerase originating from any vertebrate and any fragments of any vertebrate telomerase or fragments that are of 10-100 amino acid in length.

While methods of gene cloning, deleting and expressing, as well as testing telomerase activity, are well known in the relevant art, and skills of the artisans highly developed, isolating the telomerase gene from all vertebrate, modify them so that they encoded any protein fragments or 10-100 amino acid fragments, producing said telomerases or their fragments in host cells and isolating them is outside the realm of routine experimentation. The probability of success in obtaining the claimed invention is very low.

The only example provide by disclosure is the human telomerase variant described by SEQ ID NO:46, and the protein fragments that may be encoded by introns of SEQ ID NO: NO:18, 23, 25, 27, 29, 30, 32 and 33, which is insufficient to put one of skill in the art in possession of the attributes and features of telomerases from all vertebrates and fragments thereof. Isolating the telomerase gene from all vertebrate and modify them so that they encoded any protein fragments or 10-100 amino acid fragments, producing telomerase or its fragments in host cells and isolating polypeptides is outside the realm of routine experimentation. The probability of success in obtaining the claimed invention is very low. Applicants did not provide any guidance or example of which vertebrate to chose for gene isolation and how to perform the gene deletion so as to obtain claimed fragments. Without the further guidance on the part of Applicants as to which organism to chose and how many and which nucleotides to

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delete from the gene so as to express the claimed polypeptides, experimentation left to those in the art is improperly extensive and undue.

Claim 18 is rejected because the specification, while being enabling for the variant of human telomerase described by SEQ ID NO:46, does not reasonably provide enablement for any variants of SEQ ID NO: 6, see paragraph 2.3.1, rejection for lack of written description. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The claim is broader than the enablement provided by the disclosure with regard to the extremely large number of proteins that are variants of protein described by SEQ ID NO:46.

The nature and breath of the claimed invention encompasses any variant of the protein encoded by SEQ ID NO:46 that may result from substitution, deletion and insertion of any number of amino acid by any number of any amino acid.

While methods of gene mutation and expressing mutated proteins are well known in the relevant art, and skills of the artisans highly developed, performing modifications of SEQ ID NO:46 within the scope determined by the language of the claim is outside the realm of routine experimentation. No one skilled in the art is able to perform all possible modification of SEQ ID NO:46. In addition, the probability of success in obtaining the claimed invention is low.

The only example provided by disclosure is the human telomerase described by SEQ ID NO:46, which is insufficient to put one of skill in the art in possession of the attributes and features of all variants of said protein. Applicants did not provide any

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guidance or example how to modify SEQ ID NO:46 to obtain its required variants. Without the further guidance on the part of Applicants as to how, and which amino acid residues to change, experimentation left to those in the art is improperly extensive and undue.

Deleting the phrase "or variant thereof" from the claim would vacate this rejection.

2.4. 35 USC section 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claim 16-19 and 22 are rejected under 35 U.S.C. 102(e) as being anticipated by Cech et al in the US Patent No. 6,093,809 ('809) issued on ~~Oct.~~ July 25, 2000, with priority to Oct. 1996.

The claims are directed to an isolated protein comprising a vertebrate telomerase (claim 16), to any fragment of a vertebrate telomerase (claim 19) or any fragment that is 10-100 amino acid long (claim 22), or to the human telomerase (claim 17), or a protein comprising SEQ ID NO:46 (claim 18).

Cech et al disclose the human telomerase protein in SEQ ID NO:225. The sequence is identical to the sequence of human telomerase protein of the instant

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application (SEQ ID NO:2). The subject matter and the scope of claims 16-19 and 22 are encompassed by the disclosure of '809.

SEQ ID NO 46 of the instant application which is the human telomerase lacking the α intron, is comprised by the protein, which is the whole human telomerase. Changing the language of claim 18 from "comprising" to "consisting of" would vacate this rejection.

3. Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.


If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

Malgorzata A. Walicka, Ph.D.

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Assistant Patent Examiner


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